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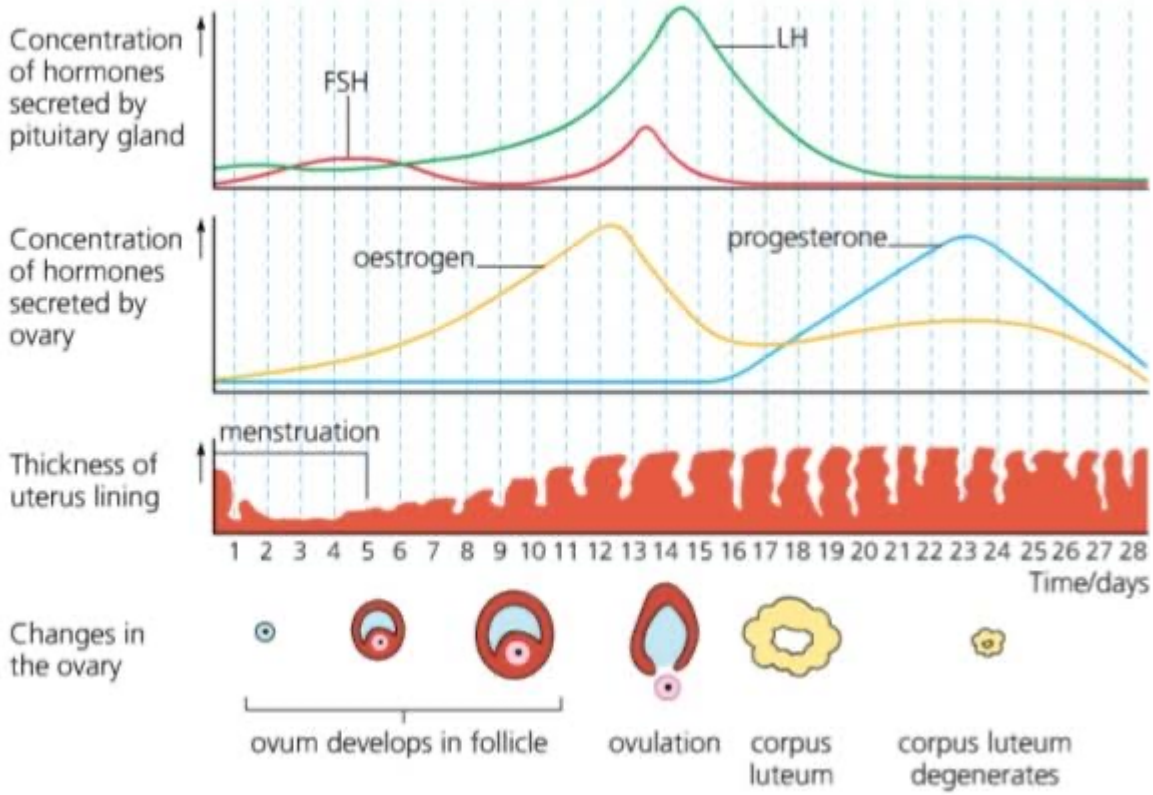
The Cyclic Changes In The Vagina

In the course of the reproductive cycle, the vaginal epithelium is subject to normal, cyclic changes, that are influenced by estrogen: with increasing circulating levels of the hormone, there is proliferation of epithelial cells along with an increase in the number of cell layers. As cells proliferate and mature, they undergo partial cornification. Although hormone induced changes occur in the other tissues and organs of the female reproductive system, the vaginal epithelium is more sensitive and its structure is an indicator of estrogen levels. Some Langerhans cells and melanocytes are also present in the epithelium. The epithelium of the ectocervix is contiguous with that of the vagina, possessing the same properties and function. The vaginal epithelium is divided into layers of cells, including the basal cells, the parabasal cells, the superficial squamous flat cells, and the intermediate cells. The superficial cells exfoliate continuously and basal cells replace the superficial cells that die and slough off from the stratum corneum. Under the stratus corneum is the stratum granulosum and stratum spinosum. The cells of the vaginal epithelium retain a usually high level of glycogen compared to other epithelial tissue in the body. The surface patterns on the cells themselves are circular and arranged in longitudinal rows. The epithelial cells of the uterus possess some of the same characteristics of the vaginal epithelium.

The Cyclic Changes In The Breast

Each month, women go through changes in the hormones that make up the normal menstrual cycle. The hormone estrogen is produced by the ovaries in the first half of the menstrual cycle. It stimulates the growth of milk ducts in the breasts. The increasing level of estrogen leads to ovulation halfway through the cycle. Next, the hormone progesterone takes over in the second half of the cycle. It stimulates the formation of the milk glands. These hormones are believed to be responsible for the **cyclical changes** that many women feel in their breasts just before menstruation. These include swelling, pain, and soreness.

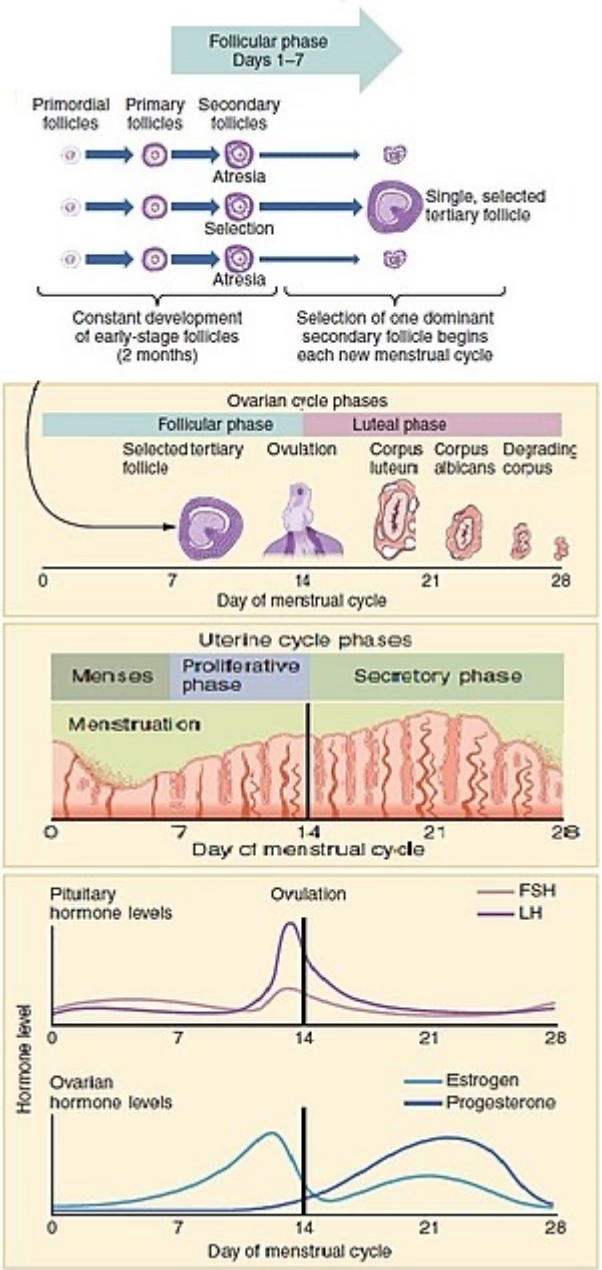
During menstruation, many women also have changes in breast texture. Their breasts may feel very lumpy. This is because the glands in the breast are enlarging to get ready for a possible pregnancy. If pregnancy does not happen, the breasts go back to normal size. Once menstruation starts, the cycle begins again.



MENSTRUAL CYCLE

The **menstrual cycle** is the regular natural change that occurs in the female reproductive system(specifically the uterus and ovaries) that makes pregnancy possible.

A female's menstrual cycle occurs to allow for oocyte release and prepare the uterus for possible pregnancy. It begins at puberty, ranging from the ages of 10 to 16, and ends at menopause at an average age of 51. It may last anywhere from 21 days to 35 days with an average duration of 28 days.



FUNCTION

Hormones are secreted in a negative and positive feedback manner to control the menstrual cycle. Hormone secretion begins in the hypothalamus where gonadotropin-releasing hormone (GnRH) is secreted in an increased, pulsatile fashion once puberty starts. GnRH is then transported to the anterior pituitary where it activates its 7-transmembrane G-protein receptor. This provides a signal to the

anterior pituitary to secrete stimulating follicle hormone (FSH) and luteinizing hormone (LH). FSH and LH provide input to the ovaries. Within the ovarian follicle, there are 2 cell types responsible for hormone production, theca cells, and granulosa cells. LH stimulates theca cells to produce progesterone and androstenedione by activating the enzyme, cholesterol desmolase. Once androstenedione is secreted, the hormone diffuses to the nearby granulosa cells. Here, FSH stimulates the granulosa cells to convert androstenedione to testosterone then 17-beta-estradiol by activating the enzyme, aromatase. As levels of 17-beta-estradiol or progesterone increase based on the phases of the menstrual cycle, there is negative feedback back to the anterior pituitary to lower the levels of FSH and LH being produced and subsequently, the levels of 17-beta-estradiol and progesterone produced. An exception to this is during ovulation, in this case, once a critical amount of 17-beta-estradiol is produced it provides positive feedback to the anterior pituitary to produce increased amounts of FSH and LH. This feedback system is represented in figure 1. Additionally, within the feedback system, the granulosa cells produce inhibin and activin, which inhibit and stimulate FSH release from the anterior pituitary, respectively. This feedback mechanism is controlled by upregulating, to increase hormone production, or downregulating to decrease hormone production, the GnRH receptors on the anterior pituitary.

MECHANISM

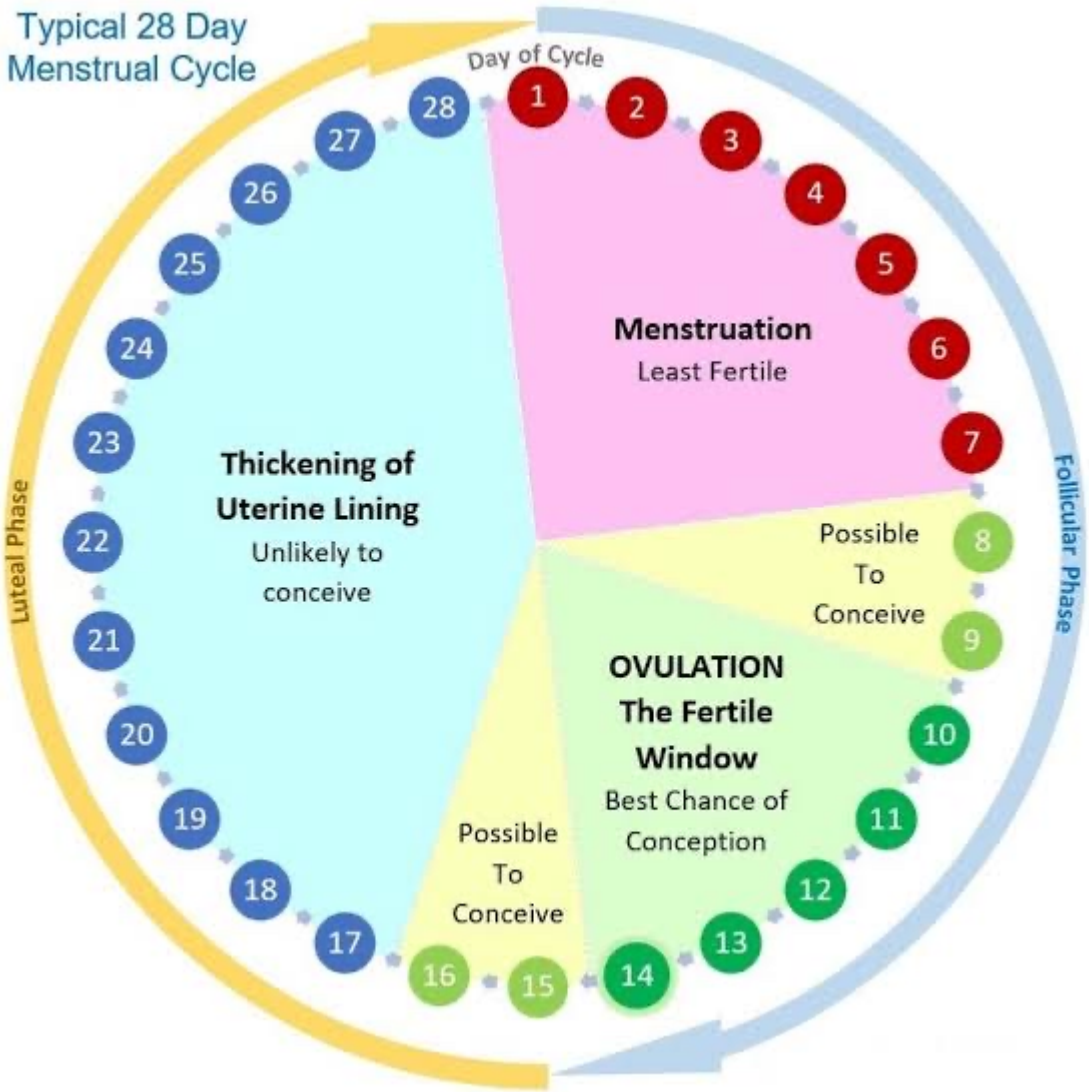
- **Phase 1: The Follicular, or Proliferative Phase**

The first phase of the menstrual cycle is the follicular or proliferative phase. It occurs from day zero to day 14 of the menstrual cycle, based on the average duration of 28 days. The variability in length of the menstrual cycle occurs due to variations in the length of the follicular phase. The main hormone during this phase is estrogen, specifically 17-beta-estradiol. The increase in this hormone occurs by up-regulation of the FSH receptors within the follicle at the beginning of the cycle. However, as the follicular phase progresses to the end, the increased amounts of 17-beta-estradiol will provide negative feedback to the anterior pituitary. The purpose of this phase is to grow the endometrial layer of the uterus. 17-beta-estradiol achieves this by increasing growth of the endometrial layer of the uterus, stimulating increased amounts of stroma and glands, and increasing the depth of the arteries that supply the endometrium, the spiral arteries. Additionally, this phase is also important to create an environment that is friendly and helpful to possible incoming sperm. 17-beta-estradiol achieves this by creating channels within the cervix allowing for sperm entry. The channels are made within the abundant, watery and elasticity changes of the cervical mucous. During this phase, a primordial follicle begins to mature to a Graafian follicle. The surrounding follicles begin to degenerate which is when the Graafian

follicle becomes the mature follicle. This sets up the follicle for ovulation, the next step.

OVULATION

Ovulation always occurs 14 days before menses; therefore, with an average 28-day cycle, ovulation occurs on day 14. At the end of the proliferative phase, 17-beta-estradiol levels are at a high due to the follicle maturation and increased production of the hormone. During this time only, 17-beta-estradiol provides positive feedback for FSH and LH production. This occurs when a critical level of 17-beta-estradiol is reached, at least 200 picograms per milliliter of plasma. The high levels of FSH and LH present during this time is called the LH surge. As a result, the mature follicle breaks, and an oocyte is released. The changes to the cervix as initiated during the follicular phase further increases allowing for increased, waterier cervical mucous to better accommodate the possible sperm. The levels of 17-beta-estradiol fall at the end of ovulation.



- **Phase 2: The Luteal or Secretory Phase**

The next phase of the menstrual cycle is the luteal or secretory phase. This phase always occurs from day 14 to day 28 of the cycle. Progesterone stimulated by LH is the dominant hormone during this phase to prepare the corpus luteum and the endometrium for possible fertilized ovum implantation. As the luteal phase ends, progesterone will provide negative feedback to the anterior pituitary to decrease FSH and LH levels and subsequently, the 17-beta-estradiol and progesterone levels. The corpus luteum is a structure formed in the ovary at the site of the

mature follicle rupture to produce 17-beta-estradiol and progesterone, which is predominate at the end of the phase due to the negative feedback system. The endometrium prepares by increasing its vascular supply and stimulating more mucous secretions. This is achieved by the progesterone stimulating the endometrium to slow down endometrial proliferation, decrease lining thickness, develop more complex glands, accumulate energy sources in the form of glycogen, and provide more surface area within the spiral arteries. Contrary to the cervical mucous changes seen during the proliferative phase and ovulation, progesterone decreases and thickens the cervical mucous making it non-elastic, since the fertilization time period passed, and sperm entry is no longer a priority. Additionally, progesterone increases the hypothalamic temperature, so body temperature increases during the luteal phase. Near the end of the secretory phase, plasma levels of 17-beta-estradiol and progesterone are produced by the corpus luteum. If pregnancy occurs, a fertilized ovum is implanted within the endometrium, and the corpus luteum will persist and maintain the hormone levels. However, if no fertilized ovum is implanted, then the corpus luteum regresses, and the serum levels of 17-beta-estradiol and progesterone decrease rapidly.

MENSES

When the hormone levels decrease, the endometrium layer as it has been changed throughout the menstrual cycle is not able to be maintained. This

is called menses, considered day 0 to day 5 of the next menstrual cycle. The duration of menses is variable. Menses or menstrual bleeding is when there is sloughing of the endometrial lining and its blood. To continue the process of the menstrual cycle, primordial follicles begin to develop and start the follicular phase again in hopes of a pregnancy.

CLINICAL SIGNIFICANCE

A female has an average of 450 menses throughout her lifetime; therefore, it is important to understand the menstrual cycle and its physiology because of the various complications, consequences, and distress that it may have for a female patient. A female presenting with primary or secondary amenorrhea will need to undergo clinical testing to diagnose the reason, but reasonable testing from the level of the ovaries to the hypothalamus cannot be performed unless a clinician thoroughly understands the hormone feedback system. Additionally, there may be problems with her menses itself such as premenstrual syndrome, dysmenorrhea, or menorrhagia. Without an understanding of the female anatomy and menstrual cycle physiology, a clinician would be unable to obtain a complete history and physical to allow understanding of the underlying cause. Infertility is a prominent issue in our society, and the menstrual cycle is the basis for how a woman's body prepares for pregnancy, so each patient's menstrual cycle must be evaluated as a possible area of concern for her infertility. As clinicians, we must

understand the menstrual cycle in its entirety to provide relevant clinical care to our female patients.